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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
09/047,652	03/25/98	[illegible]	[illegible]

HM22/1007

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EXAMINER	
[illegible]	
ART UNIT	PAPER NUMBER
1642	8

DATE MAILED: 09/07/99

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 6/16/99

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-47 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1, 4, 20, 37, 39, 43 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

+ Seq. Rule Compliance

☒ Notice of Reference Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLLOWING PAGES –

Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence

Applicant's election with travesre of group III, claims 1, 4, and 20 in Paper No.7 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant adds new claims 37-47, which are related to claims 1-36, and are not new matters. Applicant requests that new claims 40-42 to be added to claims 1, 4, and 20. After consideration of the request, claims 40-42 are not added to the elected claims 1, 4, and 20, because claims 1, 4, and 20 are drawn to a composition, whereas claims 40-42 are drawn to a method. The reasons for restricting composition claims from method claims have been recited in the earlier Office Action, paper No:6. Briefly, the products of group III could be used for different processes. New claims 37, 39, and 43 however are added to the elected claims 1, 4, and 20, because claims 37, 39, and 43 are composition claims and are related to claims 1, 4 and 20.

Accordingly, claims 1, 4, 20, 37, 39, and 43 are being examined in this instant application.

SEQUENCE RULE COMPLIANCE

The examiner acknowledges receiving a substitute paper and computer readable form of the Sequence listing. Although applicant states that the substitute paper and computer readable

form of the Sequence listing do not contain new matter, applicant fails to state that the substitute paper and computer readable form of the Sequence listing are the same. A statement that the substitute paper and computer readable form of the Sequence listing are the same is required.

REJECTION UNDER 112, SECOND PARAGRAPH

Claims 20, 37, 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 20, 37, 39 are indefinite for the use of the abbreviated language "PBR", which is not commonly used in the art. A full name of PBR is required to ~~obviate~~ obviate this rejection.

REJECTION UNDER 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1, 4, 20, 37, 39, and 43 are rejected under 35 U.S.C. 102(a) as being anticipated by Papadopoulous V. et al, 1111997, JBC, 272: 32129-32135.

Claims 1, 4, 20, 37, 39, and 43 are drawn to an antagonist of peripheral-type benzodiazepine receptors (PBR), or a natural or synthetic inhibitor of PBR function, or expression, for reducing cell proliferation or for reducing cancer growth.

Papadopoulous et al teach replacement vectors which mutate the PBR gene, suppress PBR mRNA, and nullify the presence of the 18 kDa PBR protein. Thus the replacement vectors taught by Papadopoulous et al would inherently nullify any action of the receptor PBR, because the presence of PBR protein, which is necessary for its action, is nullified by the mutation. Since an antagonist of a receptor is a drug or an agent that nullifies the action of a receptor, the .replacement vectors taught by Papadopoulous et al is an antagonist of PBR, and is the same as the claimed antagonist.

2. Claims 1, 4, 20, 37, 39, and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Mosser, PC, 1993, Drug Development Res, 30(4): 213-218, or Garnier, M et al, 1993, Endocrinology, 132(1): 444-458.

Claims 1, 4, 20, 37, 39, and 43 are drawn to an antagonist of peripheral-type benzodiazepine receptors (PBR), or a natural or synthetic inhibitor of PBR function, for reducing cell proliferation or for reducing cancer growth.

Moser et al teach the antagonist Ro 5-4864 of peripheral-type benzodiazepine receptors.

Garnier et al teach that having similar effect as polypeptide dazepam binding inhibitor (DBI), Ro5-4864, at high concentration, inhibits Leydig tumor cell growth.

Thus the composition taught by Moser et al or Garnier et al is the same as the claimed composition, i.e. a natural or synthetic PBR antagonist, which inhibits the function PBR. Since these claims are composition claims, the intention for use of the claimed composition, i.e. to stimulate cell or tumor growth, does not have any patentable weight for the purpose of comparison of the claims with the prior art.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH

Claims 1, 4, 20, 37, 39, 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an inhibitor of PBR gene expression by homologous recombination, for reducing the metastasis of a rat tumor cell line, does not reasonably provide enablement for an antagonist of PBR for reducing cancer growth. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 1, 4, 20, 37, 39, 43 are drawn to an antagonist of peripheral-type benzodiazepine receptors (PBR), or a natural or synthetic inhibitor of PBR function, for reducing cancer growth.

Claims 1, 4, 20, 37, 39, 43 are not enable because it is unpredictable whether an antagonist of peripheral-type benzodiazepine receptors (PBR), or a natural or synthetic inhibitor of PBR function, could be used for reducing cancer growth. The art teaches that, at different concentration, an antagonist of PBR, Ro5-4864, has an opposite effect on Leydig tumor cells growth (Garnier et al, 1993, *supra*). At low concentration, Ro5-4864 stimulate tumor cell growth, and at high concentration, Ro5-4864 reduces tumor cell growth. Furthermore, the

specification discloses that at low nanomolar, another antagonist of PBR, PK11195, shows no effect on MDA-231 cell proliferation, whereas at -8M, PK11195 stimulates MDA-231 cell proliferation (example 3). Even by suppresion of the expression of PBR by homologous recombination, only metastasis is inhibited, but invasive breast tumors still invade and grow locally (example 7). Thus depending on the type of antagonists of PBR, and depending on their concentrations, opposite effects of the antagonist on tumor cell growth could be obtained. Yet the claims and the specification do not specify the concentration, nor the type of antagonist of PBR, wherein the tumor cells are exposed to, and are reduced in growth. The specification fails to provide an enabling disclosure for how one would use an antagonist of PBR for inhibiting tumor growth, in view of the presence of a large number of antagonists of PBR, in view of contradictory effects of different types antagonists, and further in view of contradictory effects of different concentrations of a given antagonists. The specification provides insufficient guidance with regards to these issues, and provides no working examples, which would provide guidance to one skilled in the art on how to use the broadly claimed composition. Although a working example is usually not required, but in view of the above unpredictability, undue experimentation would be required to use the claimed composition.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Minh-Tam B. Davis whose telephone number is (703) 305-2008. The

examiner can normally be reached on Monday-Friday from 10:00 am to 2:00 pm, except on Wesnesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached on (703) 308-4310. The fax phone number for this Group is (703) 308-4227.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**Paula.Hutzell@uspto.gov**].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless **the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122.** This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0916.

Minh-Tam B. Davis

August 12, 1999

PAULA K. HUTZELL
SUPERVISORY PATENT EXAMINER